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ORIGINAL ARTICLE

Comparison of the effects of remifentanil and alfentanil on intraocular pressure in cataract surgery

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ABSTRACT

Background: Anesthesia for ophthalmic surgery requires management of intraocular pressure (IOP) during perioperative period. In an open eye, in conditions such as after traumatic injury or during cataract surgery, IOP increase can lead to permanent vision loss. Administration of narcotics concomitant with anesthetics has the ability to reduce this increase of IOP. This clinical trial aims to compare the efficacy of remifentanil and alfentanil in preventing an increase in IOP after administration of succinylcholine, intubation and during anesthesia. **Methods:** This double-blind clinical trial was conducted on 50 patients undergoing elective general surgery for cataracts. Patients were randomly divided into two groups. Alfentanil (20 μg/kg in 30 s) for group 1 and remifentanil (1 μg/kg in 30 s) for group 2 were injected before induction of anesthesia, and 0.5 μg/kg/min alfentanil for group 1 and 0.1 μg/kg/min remifentanil for group 2 were infused during the anesthesia. Systolic and diastolic blood pressure, heart rate, and IOP from normal eye were measured before the induction, after administration of thiopental and succinylcholine, after tracheal intubation, and 2 min later, and were repeated in 2-min intervals until the end of operation. **Results:** IOP decreased after injection of anesthetics and remained lower all through the operation in both groups, but IOP decreased after injection of succinylcholine in remifentanil group while it increased in alfentanil group ($P<0.05$). **Conclusions:** Results of this study indicate benefits of both remifentanil and alfentanil in managing IOP after induction and during anesthesia. It seems that remifentanil is better than alfentanil in controlling the IOP after injection of succinylcholine.

Key words: *Alfentanil, anesthesia, cataract surgery, intraocular pressure, remifentanil*

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INTRODUCTION

Increasing intraocular pressure (IOP)[1] in intraocular surgery operations has always been problematic for the surgeon and it is necessary to prevent the elevation of IOP and control it in normal range. In general, anesthesia management in ophthalmic surgery requires IOP controlling before, during, and after the surgery.

Normal IOP value is approximately 12-20 mmHg, which is associated with periodic oscillation of about 2-3 mmHg, and it changes by about 1-6 mmHg dependent to the status.

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The main factors affecting the IOP are related to aqueous humor dynamics, changes in choroidal blood volume[2], central venous pressure, and extraocular muscle tone. Events such as coughing, straining, Valsalva maneuver, or vomiting can cause temporary, but significant increase in IOP.[1]

Sudden increase in systolic arterial blood pressure could cause temporary increase in IOP and choroidal blood volume (CBV).

Laryngoscopy and intubation lead to a rise of 10-20 mmHg in IOP, and this may be prevented by avoiding the hypertensive response to intubation and extubation.[2]

Succinylcholine is used to facilitate rapid tracheal intubation in patients at risk of aspiration of gastric contents. However, succinylcholine injection and consequently tracheal intubation is associated with increased IOP.[3]

1. Intraocular pressure
2. Choroidal blood volume (CBV)

IOP rise after injection of succinylcholine occurs as a result of its effect on CBV or formation of aqueous humor and is dependent upon the dose and time of injection. During anesthesia, increasing IOP can lead to permanent vision loss.

After opening the globe in surgery, IOP equals to the atmospheric pressure, and any sudden increase in eye pressure can lead to prolapse of the iris and lens and cause the vitreous to be discharged and reduced.[4]

Medications such as inhaled anesthetics, sedatives, barbiturates, etomidate, and propofol, and opioids such as remifentanil, sufentanil, and alfentanil reduce IOP. Opioids and anesthetic drugs can reduce extraocular muscle tone, weaken the central nervous system, improve aqueous humor drainage, reduce aqueous humor production and arterial and venous blood pressure, and thereby can cause IOP reduction.[1]

There are several pre-treatment regimens in controlling sympathetic responses to tracheal intubation, and the injection of rapid-acting opioids before anesthesia is more common among them.[5]

Various studies have focused on the effects of opioids in preventing IOP rise following the injection of succinylcholine and laryngoscopy and tracheal intubation. The results obtained from these studies indicate a favorable effect of using fast-acting opioids such as remifentanil and alfentanil to prevent the IOP increase.[6-8]

Alfentanil modifies increased IOP following the injection of succinylcholine, laryngoscopy and tracheal intubation, but it might be associated with respiratory depression, particularly in the elderly.[9]

Remifentanil is a μ receptor agonist with short effect, which has a rapid onset of analgesia, and only 1 min after injection, its maximal effect appears. Due to its rapid metabolism, respiratory depression will also be shorter[10] and it can be a good alternative to alfentanil.[3]

The purpose of this study is to compare the effects of remifentanil and alfentanil in moderating IOP increase, followed by tracheal intubation and succinylcholine injection in cataract surgery (for patients with long-lasting surgery) as a clinical trial.

METHODS

After the approval of university ethical committee and written consent from patients to be studied were obtained, 50 patients with physical condition of American Society of Anesthesiologists (ASA)[3] I-II, who were scheduled for elective cataract surgery, were studied in a double-blind clinical trial. Patients with hypertension, cardiovascular and eye disease, taking vasoactive drugs, suffering from glaucoma, taking ophthalmic drugs, and having airway problems were excluded from the study due to the likely effect on IOP.

Randomly classified patients were placed into two groups of 25 people each: Remifentanil (R) and alfentanil (A).

Before the induction of anesthesia, 1 μg/kg bolus dose of remifentanil in 30 s in the R group and 20 μg/kg of alfentanil in the A group were injected. In the management of anesthesia, remifentanil infusion (0.1 μg/kg/min) or alfentanil infusion (0.5 μg/kg/min) was used. Induction of anesthesia was performed by sodium thiopental (5 mg/kg) and endotracheal intubation was facilitated by using succinylcholine (1 mg/kg). After intubation, anesthesia was maintained with 100 μg/kg/m propofol infusion, along with the inspiratory gas mixture (50% oxygen and 50% N2O). To maintain muscle relaxation during surgery, 0.1-0.2 mg/kg atracurium was injected and the patients were mechanically ventilated during surgery. Systolic and diastolic blood pressure and heart rate were measured and recorded by an anesthesiologist before induction of anesthesia, 30 s after injection of sodium thiopental, 30 s after injection of succinylcholine, immediately after tracheal intubation, 2 min after tracheal intubation, and at 2 min intervals until the end of surgery.

At the mentioned times, IOP was measured by an ophthalmologist (other than surgeon) on the eye in which surgery was not performed.

None of the drug-prescribing anesthesiologists or the ophthalmologist responsible for measuring IOP was aware of any drugs prescribed to patients.

Finally, the data were segregated as systolic and diastolic blood pressure, mean arterial pressure (MAP), heart rate, and IOP, and all criteria were investigated as increase or decrease from base rate at determined times. To achieve more reliable results regarding IOP, all the patients were ventilated mechanically with an equal respiratory rate (12/min) and tidal volume (10 ml/kg). Blood pressure and saturation of oxygen were measured by equal monitoring device, and IOP was measured by using Schiotz tonometer.

Sample size was calculated to detect a mean IOP difference of 4 mmHg[3] between remifentanil and control groups by α=0.05 and β=20% (in accordance with the sample size calculation formula), about 20 people for each group. To

3. American Society of Anesthesiologist

obtain more confidence, 25 people were enrolled in each group.

Basal quantitative data were analyzed with Student's *t*-test for independent groups, and Chi-square or Fisher's exact test (FET) was used for comparing qualitative data. To compare the average of IOP changes, and blood pressure and heart rate in both groups during the different stages of anesthesia, we used analysis of variance (ANOVA) test with two-variable repeated measure form (Bonferroni procedure). The results were analyzed using statistical software SPSS version 15 and the significance level was considered to be less than 0.05.

RESULTS

A comparison of demographic characteristics and the average basal IOP values and hemodynamic signs in the two groups did not show significant differences [Table 1]. IOP in both groups had significantly decreased after injection of sodium thiopental and had slightly increased after injection of succinylcholine in the alfentanil group, and again it fell in the remifentanil group [Figure 1]. Immediately after tracheal intubation in both groups, IOP increased, but in none of the two groups, IOP reached the basal values until the end of surgery. In terms of IOP, the difference between the two groups was only significant after the injection of succinylcholine (P=0.004), and at other stages the two groups' mean IO*P* values were not significantly different (P>0.05). The comparison of average of MAP changes between the two groups in different stages has been shown in Figure 2. This analysis showed that the MAP between the two groups in various stages had no significant differences (P<0.05). In terms of heart rate, the two groups of alfentanil and remifentanil had no significant difference until the second minute after tracheal intubation (P>0.05), but in the fourth minute after intubation, heart rate decreased in the alfentanil group, whereas it increased in the remifentanil group [Figure 3] and the difference between

Table 1: Basic characteristics of patients; mean (SD)

Variables	Alfentanil group	Remifentanil group	*P* value
Age (years)	67.5 (7.5)	70.7 (8.2)	0.15
Gender (male/female)	16/9	17/8	0.76
Duration of operation (min)	21.2 (3.1)	19.7 (3.8)	0.14
Intraocular pressure (mmHg)	15.1 (1.6)	14.7 (2.6)	0.51
Heart rate (bpm)	76.6 (13.2)	78.8 (6.8)	0.45
Systolic blood pressure (mmHg)	139.6 (26.2)	136.8 (22.5)	0.68
Diastolic blood pressure (mmHg)	80 (19.8)	82.6 (11.2)	0.57
Mean arterial pressure (mmHg)	119.7 (22.6)	118.7 (18.1)	0.86

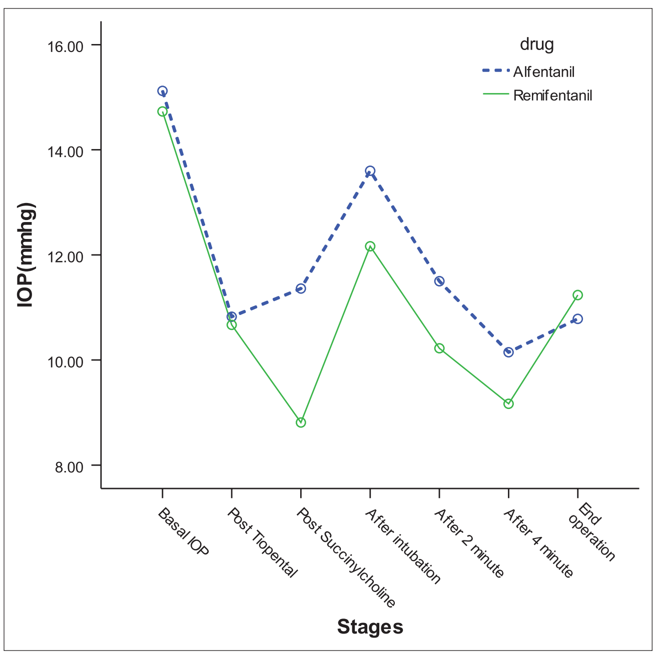

Figure 1: Comparison of intraocular pressure (IOP) changes between the two groups of alfentanil and remifentanil at different stages of anesthesia

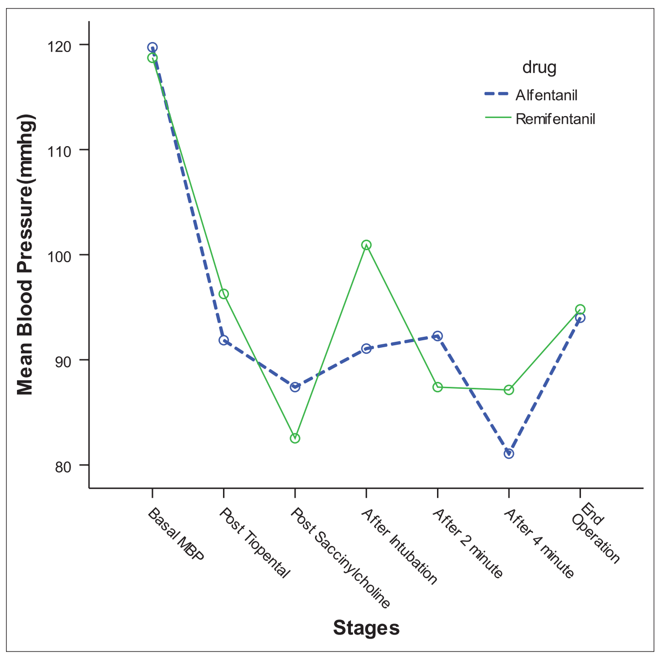

Figure 2: Comparison of changes in mean arterial pressure between the two groups of alfentanil and remifentanil at different stages of anesthesia

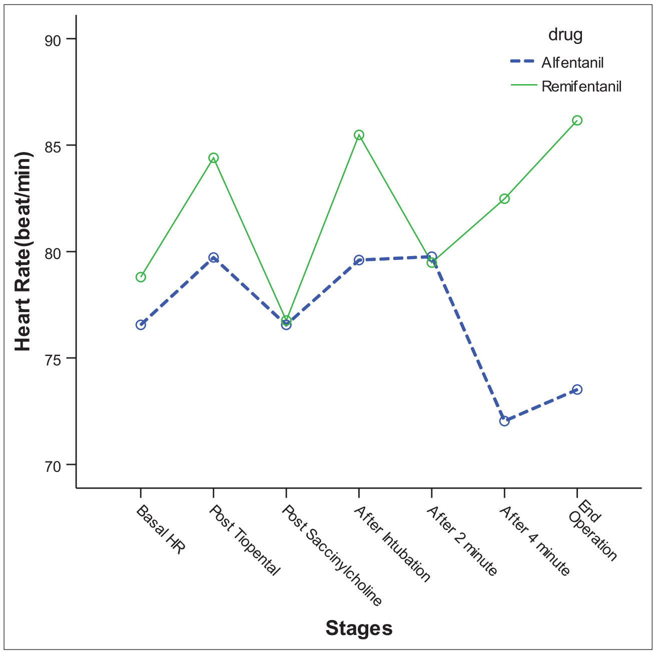

Figure 3: Comparison of heart rate changes between the two groups of alfentanil and remifentanil at different stages of anesthesia

these two groups was significant (P=0.008). In addition, at the end of surgery, we could observe significant differences in the heart rate between the two groups (P=0.001).

DISCUSSION

According to rapid-acting effect after injection, succinylcholine is widely used as a muscle relaxant drug in a rapid sequence induction of anesthesia. Several studies indicate an increase in IOP from basal values after administration of succinylcholine, and the use of this drug is limited in case of damage to the eye.[11] Increasing IOP after administration of succinylcholine may depend on various factors such as the injection time, dose rate, contraction of muscle fibers of extraocular muscles, or a direct effect of succinylcholine on choroid blood volume or production of aqueous humor.[9] The risk of vitreous fluid depletion as a result of increasing ocular pressure should be compared against the risk of aspiration of gastric contents. However, previous studies indicate further increases in IOP due to conducting laryngoscopy and tracheal intubation.[12] Both remifentanil and alfentanil can prevent ocular pressure increase. These drugs can reduce IOP by relaxing the internal ocular muscles and facilitating the removal or reduction of aqueous humor production.[3] In this study, following the injection of succinylcholine, the IOP had increased in alfentanil group but decreased in remifentanil group. This could be due to the onset of rapid-acting remifentanil, which creates maximal decline in IOP at the time of administering succinylcholine and tracheal intubation. Moreover, laryngoscopy and tracheal intubation in both groups had increased the IOP level, but in none of the two groups this increase was up to the basic values. Zimmerman and colleagues in their study on 60 patients in three groups showed that in all patients after induction of anesthesia, IOP was decreased, while it was increased following the injection of succinylcholine and tracheal intubation. However, adding alfentanil to anesthesia drugs could keep the IOP under the basal values and lower than other groups during all the stages of surgery.[11] Eti and colleagues in a study on 40 patients showed that adding alfentanil to anesthesia drugs caused the IOP to stay lower and not to increase after injecting succinylcholine and performing laryngoscopy and tracheal intubation.[7] In another study on 30 patients in 1998, Alexander and colleagues found that compared to the control group, patients who had received remifentanil along with anesthetic drugs not only had no IOP increase after receiving succinylcholine and tracheal intubation, but also had some reduction in IOP level.[3] The comparison of the two drugs "fentanyl and remifentanil" by Ng and colleagues showed that compared with fentanyl, remifentanil could control IOP increase following the injection of succinylcholine and tracheal intubation, and it could be a more useful drug in patients with ocular trauma.[8] Moreover, the comparison of these two drugs in Sator *et al.*'s study indicates that compared with fentanyl, remifentanil has some superiority in terms of the greater stability on IOP during the surgery.[6] Remifentanil at a dose of 1 μg/kg could cause the maximal decrease in IOP only 1 min after the injection, and thereby its injection along with other inducting anesthesia drugs in rapid sequence induction facilitates laryngoscopy and tracheal intubation. It prevents blood pressure increasing responses as well as IOP increase following laryngoscopy and tracheal intubation.[3] The results of these studies show that although both alfentanil and remifentanil modify IOP increase resulting from succinylcholine and tracheal intubation, remifentanil has better effects after injecting succinylcholine and tracheal intubation. This advantage is considerable in our study, too. In addition, in terms of changes in MAP, significant difference between the two drugs in all surgical stages was not observed, which is consistent with the findings of other studies.[3,7]

CONCLUSION

In general, this study shows that following the injection of succinylcholine and tracheal intubation, remifentanil can prevent IOP increase with minimal hemodynamic changes. Also, its use along with anesthetic drugs can be considered in patients with ocular trauma.

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